Electrical Cardioversion

Effectiveness of Quinidine Prophylaxis Following Countershock

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■ *Direct current countershock was given to 46 patients with chronic atrial fibrillation of diverse causes, with successful conversion in 87 per cent of them. Patients were observed while receiving quinidine prophylaxis, with serial determination of serum quinidine levels, for up to 22 months. Two quinidine preparations were employed, one a long-acting form, in various dosage regimens and both preparations were found to be effective prophylactic agents for maintaining reliable serum quinidine levels. Fifty per cent of patients remained in normal sinus rhythm at three months, 28 per cent at six months and 13 per cent at twelve months.*

DIRECT CURRENT SYNCHRONIZED countershock is a considerable achievement in the treatment of chronic atrial fibrillation and other arrhythmias. Until the introduction of this electrical method for the treatment of ectopic rhythm disorders the major armamentarium included quinidine procainamide and the digitalis glycosides. It had always been recognized that biologic titration with drugs was tedious, and in addition the hazard with quinidine included a 35 per cent incidence of toxicity and a 2 per cent fatality rate.[5] Synchronized precordial electroshock has been the most significant addition to antiarrhythmic therapy since the introduction of quinidine. Notwithstanding the safety and efficacy of countershock, there are still isolated reports of such complications as embolic phenomena, cardiac standstill and ventricular fibrillation.[2,8] To prevent these possible complications, one must anticipate them by proper preparation of the patient, analysis of the ectopic mechanism and awareness of the risks.

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Direct countershock is reported in various series as being successful in terminating supraventricular arrhythmia in from 80 to 100 per cent of cases.[4,6,7] Although the arrhythmia may be terminated, maintenance of a normal sinus mechanism depends on the competency of the sinus node and, perhaps, on drug therapy. The necessity, the choice of preparations and the manner of administration of prophylactic quinidine following countershock are questions still unanswered. It would therefore seem important to assess the total value of the countershock therapy in producing long-term sinus rhythm rather than purely the immediate conversion results.

This study has three major purposes: (1) To assess the effectiveness of long-term quinidine maintenance following direct current countershock; (2) to roughly compare the effectiveness of USP Quinidine Sulfate with that of a delayed absorption quinidine preparation*; and (3) to determine if a common denominator of serum quinidine levels exists which contributes to maintaining a sinus rhythm.

*Quinidex Extentabs, supplied through the courtesy of A. H. Robins Co., Richmond, Virginia.

TABLE 1.—*Cause of Atrial Fibrillation in 48 Patients*

Cause	Number of Patients
Arteriosclerotic heart disease	18
Rheumatic heart disease	15
Thyrotoxic heart disease	2
Pulmonary heart disease	2
Myocardiopathy (Alcoholic)	2
Hypertensive cardiovascular disease	3
Luetic heart disease	1
Miscellaneous combined	5

Materials and Methods

Forty-eight patients, 28 men and 20 women, referred to the Conversion Clinic of the San Diego County University Hospital were the subjects of this study. Forty-seven of them had chronic atrial fibrillation and one had chronic atrial flutter. All had previously been stabilized for cardiac decompensation or recent myocardial infarction. Ages ranged from 28 to 84 years. The causes of arrhythmia in these patients are shown in Table 1.

In general, most patients were considered suitable candidates for countershock. However, some degree of selectivity was practiced in that the suggestions by Hurst[3] were considered relative contraindications. Excluded were patients previously found to be intolerant of quinidine because of idiosyncrasy or cinchonism, patients with atrial arrhythmias precipitated by digitalis toxicity and patients in whom reversion had been attempted more than twice before but had recurrence of arrhythmia despite quinidine prophylaxis.

Most patients were admitted 18 to 24 hours before conversion, and digitalis, diet or diuretics were continued if previously prescribed. All patients were either given sodium heparin, 10,000 units every eight hours, or continued on coumadin if previously prescribed. USP quinidine sulfate (QS) or quinidine long-acting (QX) was started by the ward physician according to a preset schedule. Quinidine sulfate was given in dosage of 200 mg either every six or every eight hours. A 300 mg long-acting quinidine tablet was given either every eight or every 12 hours. The respective medications were given at 10:00 p.m. the evening before the procedure and again at 6:00 a.m. before the conversions, which were generally performed at 7:30 a.m.

On the morning of the procedure an infusion was started of 1,000 ml of 5 per cent dextrose in water containing 40 mEq of potassium chloride and 10 mg of sodium heparin. On occasion 10 units of regular insulin was added to the infusion if borderline digitalis intoxication was suspected. A serum quinidine level was drawn at the time of the infusion and measured fluorometrically by the method of Gelfman and Seligson.[1] Serum concentrations are reported as micrograms per milliliter (quinidine base comprises 83 per cent of quinidine sulfate).

All conversions were performed in the recovery room of the operating suite. Patients were premedicated with 100 mg sodium pentobarbital or 500 mg chloral hydrate the previous evening and 100 mg meperidine with 0.4 mg atropine one hour before the procedure. Anesthesia was administered to all patients, the agent used being intravenous sodium thiopental.

Direct current countershock was delivered with the Lown Cardioverter (American Optical Company). In 35 patients the electrode paddles were applied to the right third interspace and left midaxillary line. A disc paddle was alternately used posteriorly at the left scapular tip in many instances where the left atrium was presumed to be large. The synchronizer was present for a zero delay, and a stepwise increase in capacitor discharge, starting with 150 watt seconds and rising to a maximum 400 watt seconds, was given. In no case were more than four shocks given to any patient. Following the procedure, patients were discharged either the same day or the next morning and advised to continue their prescribed quinidine. They were reevaluated in one week and then observed at monthly intervals thereafter, at which time blood quinidine levels and electrocardiograms were obtained.

Results

There were 57 conversion attempts on 46 patients* and there were 50 successes in 40 patients and seven unsuccessful attempts on six patients. Thus, 88 per cent of the conversion attempts were successful and 87 per cent of patients reverted to a normal sinus mechanism. (Interestingly, the seven unsuccessful conversions (Table 2) were in relatively young persons with severe forms of heart disease such as cardiomyopathy, hemochromatosis or rheumatic calcified annulus.)

*Two of the original 48 patients converted spontaneously on long-acting quinidine every 12 hours, one with serum quinidine levels of 1.0 mcg and the other with 2.8 mcg per ml. Both patients had prolonged follow-up and although the quinidine was discontinued from three to six months following conversion a normal sinus rhythm was maintained (Table 3). It should be noted that the table lists one conversion attempt for each patient. These are drug reversions and do not enter into the final analysis.

TABLE 2.—*Unsuccessful Conversions**

Case	Age Sex	Cause	Duration of Arrhythmia	Date of Conversion	Quinidine Level (mcg per ml)	Drug and Dosage	Number of Conversion Attempts
1	48 M	Cardiomyopathy LBBB, AF	10 years	5/64	4.2	QX 300 mg q12h	1
2	44 F	Calcified annulus RHD, MR, MS, LVH, AF	6 months	4/64	5.4	QS 200 mg q6h	1
3	55 M	? Cardiomyopathy ASHD, AF	8 years	5/65	1.2	QX 300 mg q12h	1
4	59 M	RHD, MR, LVH, AF	4 years	1/64 2/64	6.0 2.6	QS 200 mg q6h QX 300 mg q12h	2
5	68 M	Hemochromatosis ASHD, AF	8 years	3/64	2.0	QS 200 mg q6h	1
6	46 M	HCVD, LVH, AF	4 years	4/65	3.4	QS 200 mg q6h	1

*Quinidine levels represent those at the time of conversion. ASHD=arteriosclerotic heart disease; RHD=rheumatic heart disease; LVH=left ventricular hypertrophy; LBBB=left bundle branch block; HCVD=hypertensive cardiovascular disease; MR=mitral regurgitation; MS=mitral stenosis; M=male; F=female; QX=Quinidine Extentabs; QS=USP Quinidine Sulfate; AF=atrial fibrillation.

In the 46 cases in which conversion was attempted, a successful conversion was considered to be one where a normal sinus mechanism was maintained for at least one week. All patients were followed for periods varying between one week to 22 months. However, seven patients were lost to follow-up after one month. Thirty-three patients (72 per cent) remained in normal sinus rhythm at one month, 23 (50 per cent) at three months, 13 (28 per cent) at six months and six (13 per cent) at from 12 to 22 months.

Quinidine long-acting (QX) was given to 34 patients. When the dosage was 300 mg every 12 hours the average serum quinidine level was 2.4 mcg per ml. When it was given every eight hours the average serum level was 5.8 mcg per ml. At the time of conversion the mean serum level was 3.3 mcg per ml for all dosage regimens (Table 4).

USP quinidine sulfate (QS) was given to 17 patients. When the dose was 200 mg every six hours the average serum quinidine level was 3.6 mcg per ml. When 200 mg was given every eight hours the average serum level was 2.7 mcg per ml. One patient (Case 7, Table 5) was given 400 mg every six hours and the serum level was 8 mcg per ml at conversion. Eleven specimens were obtained at the time of conversion with an average serum level of 4.2 mcg per ml for all dosage regimens (Table 5).

In the seven unsuccessful conversion attempts QX was given every 12 hours to three patients and an average serum quinidine level of 2.7 mcg per ml was noted. QS was given at six hour intervals in four instances and the average serum level was 4.2 mcg per ml (Table 2).

In four patients quinidine intolerance developed, with symptoms of cinchonism—three on QX and one on QS. One patient (Case 12, Table 5) died with normal sinus rhythm four months following quinidine discontinuation. Two patients

TABLE 3.—*Spontaneous Conversions in Two Patients**

Case	Age Sex	Cause	Duration of Arrhythmia	Date of Conversion	Quinidine Level at Conversion (mcg per ml)	Quinidine Maintenance Levels (mcg per ml)	Drug and Dosage (mg)	NSR (Months)	Number of Conversion Attempts	Comments
1	58 M	RHD, AI, LVH, AF	5 mos.	4/64	1.0	3.2 3.4 2.2 7.2	QX 300 q12h	9	1	
2	73 F	Thyrotoxic ASHD, AS, LVH, AF	2 yrs.	4/64	2.8	2.0	QX 300 q12h	18	1	Quinidine discontinued 7/64.

*The quinidine levels represent those at the time of conversion and maintenance levels are those at intervals during follow-up. RHD=rheumatic heart disease; ASHD=arteriosclerotic heart disease; AI=aortic insufficiency; AS=aortic stenosis; LVH=left ventricular hypertrophy; AF=atrial fibrillation; QS=USP Quinidine Sulfate; QX=Quinidine Extentabs; M=male; F=female.

TABLE 4.—*Data on 26 Patients Given 300 mg Quinidine Extentabs (QX)**

Case	Age	Sex	Cause	Duration of Arrhythmia	Date of Conversion	Quinidine Levels Conversion (mcg per ml)	Quinidine Level at Conversion (mcg per ml)	Drug and Dosage (mg)	NSR (Months)	Number of Conversion Attempts	Comments
1	57	F	RHD, MS, AI, LVH, AF	5 years	2/64	3.2	6.6; 4.2 2.5	QX q12h QX q8h QX q12h	2	2	Intolerant. Refibrillated 4/64.
2	78	F	ASHD, Atrial Flutter	1 month	5/65	6.8	4.3	QX q8h QX q12h	1	1	
3	64	F	ASHD, MR, AI, LVH, MI, AF	3 years	9/64	5.4	2.3	QX q8h QX q12h	1	1	Intolerant. Refibrillated 10/64. Expired 1/65—CVA.
4	62	M	ASHD, MI, PE, AF	2 years	6/64	3.6	5.4	QX q12h	1	1	
5	78	M	ASHD, AS, AI, MR, AF	4 months	6/64	1.6	1.8	QX q12h	1	1	Refibrillated 7/64.
6	69	F	ASHD, MR, LVH, AF	9 years	8/64 8/64	2.2 2.3	5.9; 6.8	QX q12h QX q8h QX q12h	1	2	Refibrillated 9/64.
7	41	F	CM, AF	2 years	2/64	2.2	3.0	QX q12h	1	1	
8	57	F	RDH, MS, MR, LVH, AF	3 months	2/64	2.1	4.2; 3.1 2.3	QX q8h QX q12h	6	2	
9	36	M	RHD, MS, AI, LVH, AF	2 years	2/64	1.4	1.8; 1.8	QX q12h	4	2	
10	56	M	ASHD, Lues, AI, LVH, AF	3 months	2/64 3/64	2.4 1.6		QX q12h QX q12h	2	2	
11	36	F	RHD, MS, AF	7 months	5/65	1.0	1.0; 3.8	QX q12h	2	1	
12	64	M	Thyrotoxic AF	1 year	5/65	1.6	1.8; 2.4 2.4	QX q12h	3	1	
13	57	F	RHD, MS, MR, LVH	6 years	3/64	2.0		QX q12h		1	Died 12 hours. Autopsy—pulmonary embolus.
14	61	M	ASHD, Emph., AF	1 year	3/64	3.8	1.6; 4.8 2.8; 3.4 2.6; 4.9 2.9; 1.8	QX q12h	22	1	QX discontinued 11/64. NSR 8/65.

15.....44	M	RHD, MR, MS, LVH, AF	8 months	8/64	1.1	6.6; 7.2	QX q12h QX q8h	6	3	
				2/65		8.8				
16.....66	M	ASHD, Emph., MI, LVH, AF	6 months	11/64	2.6		QX q12h	7	3	QX discontinued 5/65. Refibrillated 5/65.
				5/65		5.6; 2.9				
				6/65				1		
17.....77	M	ASHD, MR, LVH, AF	11 months	2/65	3.0		QX q12h			
						3.8; 1.4		4		
						1.9; 2.2			2	
				5/65	1.4		QX q12h	2		
18.....65	F	RHD, MS, MR, AI, LVH, AF	6 months	8/64	4.0		QX q12h			
						4.2; 5.2		13	1	
						4.2; 4.4				
						4.9; 5.6				
19.....71	F	ASHD, MR, AF	2 years	2/64	3.0		QX q12h			QX discontinued 6/64.
						3.8; 5.2		11	3	Refibrillated 2/65.
						2.8; 2.6				
						3.8				
				2/65	3.8			1		
				3/65	3.2					
20.....55	F	RHD, AI, MR, LVH, AF	2 years	8/64	2.3		QX q12h	3		Intolerant. QX discontinued 9/64. Refibrillated 11/64. Conversion without QX unsuccessful.
						5.0			2	
				11/64			none			
21.....69	F	ASHD, MR, LVH, AF	9 years	8/64	2.2		QX q12h	1		
						5.9; 6.8	QX q8h		2	
				9/64	2.3		QX q12h	1		
22.....78	M	ASHD, MR, LVH, MI, AF	1 month	8/64	1.8		QX q12h	2	1	Died 10/64—CVA.
						1.9				
23.....53	F	RHD, LVH, AS, AI, AF	5 years	4/64	1.6		QX q12h			
						2.6; 1.8		5		
				8/64	5.0		QX q8h			
						4.0				
				9/64	4.4			1		
24.....28	M	RHD, AI, LVH, AF	6 years	3/64	8.0		QX q8h			
						2.4; 1.4	QX q12h	12	1	
						2.8; 2.4				
						3.3; 4.2				
						1.8; 4.2				
						2.8; 1.4				
25.....65	M	ASHD, AF	7 years	2/65	2.0		QX q12h	1	1	
26.....51	M	ASHD, AF	2 months	4/64	6.0		QX q8h	18		QX discontinued 4/64.

*NSR is the period of follow-up with normal sinus rhythm. ASHD=arteriosclerotic heart disease; RHD=rheumatic heart disease; Emph.=emphysema; PE=pericardial effusion; MR=Mitral regurgitation; MS=mitral stenosis; AI=aortic insufficiency; MI=myocardial infarction; AS=aortic stenosis; LVH=left ventricular hypertrophy; AF=atrial fibrillation; CVA=cerebrovascular accident; CM=cardiomyopathy; M=male; F=female.

(Cases 1 and 20, Table 4) reverted to atrial fibrillation two and three months, respectively, following discontinuation of quinidine.

There was one death in this series presumably attributable to conversion (Case 13, Table 4). The patient had severe mitral stenosis with insufficiency, atrial fibrillation of six years' duration and previously unsuccessful attempts at quinidine conversion. She died 12 hours following successful conversion, and at necropsy old massive organized bilateral pulmonary artery thrombosis was noted. In one patient (Case 9, Table 5) ventricular tachycardia developed with the first shock. Subsequently the heart reverted to normal sinus rhythm with an additional discharge.

In four patients quinidine was discontinued either immediately or up to one year following conversion. One patient (Case 16, Table 4) remained in normal sinus rhythm for eight months while on quinidine and reverted to atrial fibrillation within one week following discontinuation. Two further attempts at conversion, one without quinidine, were unsuccessful. At the time this report was being written, three patients (Cases 14 and 26 in Table 4 and Case 1 in Table 3) had gone nine, 18 and 15 months, respectively, without quinidine prophylaxis.

Comment

Our experience with the success of direct current countershock in terminating atrial fibrillation is similar to that of other observers[4-7] in that there appears to be no clear-cut relationship between the age of the patient, the duration of arrhythmia or the ease of conversion. Our experience also confirms the impression of these others that atrial fibrillation secondary to arteriosclerotic heart disease is easiest to terminate while that of rheumatic heart disease associated with left atrial hypertrophy is most difficult. Because it is impossible to predict with any degree of certainty which patients will maintain a normal sinus mechanism, it is our policy to consider all patients with atrial fibrillation as suitable candidates for conversion at least once.

Ninety-two per cent of persons who were given Long-Acting Quinidine on a 12-hour schedule maintained serum quinidine levels between 1 and 5 mcg per ml while 83 per cent of patients given USP Quinidine Sulfate on a six-hour schedule maintained serum quinidine levels of the same magnitude (see Chart 1). Of 23 patients maintaining a sinus rhythm three or more months, 13 were receiving Quinidex Extentabs,® eight were

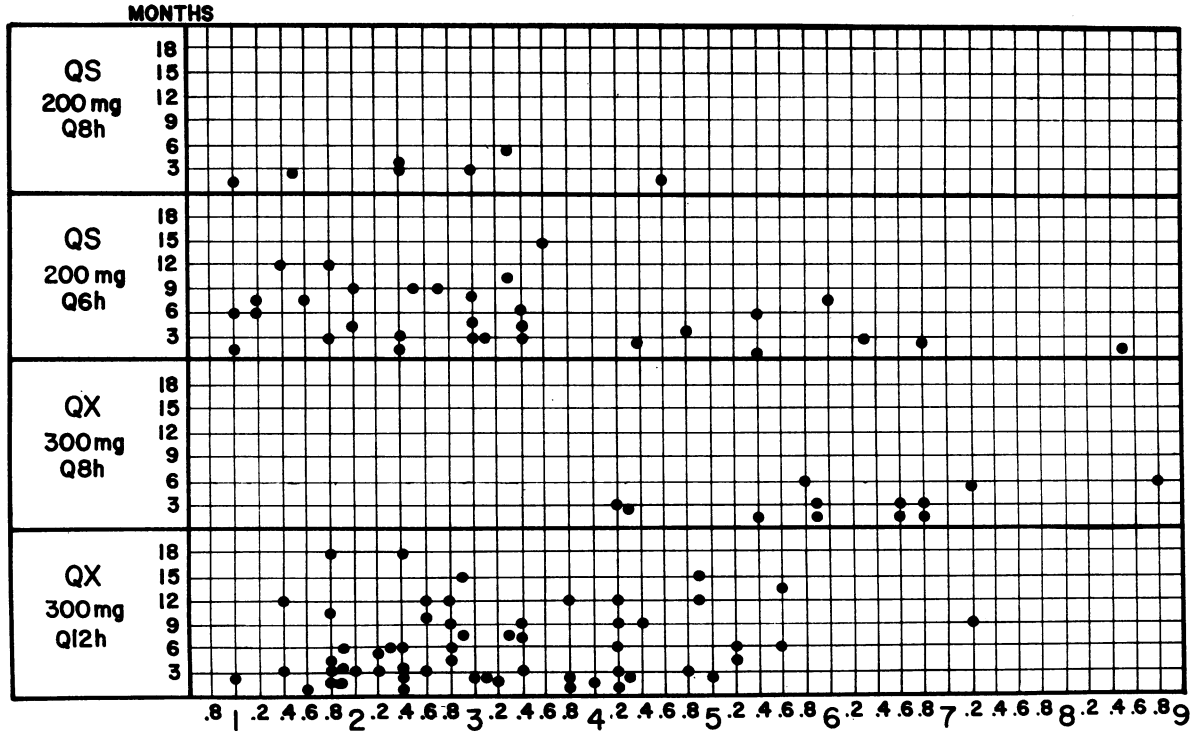

Chart 1.—Serial serum quinidine levels for all dosage regimens of both USP Quinidine Sulfate (QS) and Quinidine Extentabs (QX). The abscissa represents the serum levels in micrograms per millimeter. The ordinate represents the interval following electrical conversion in months.

TABLE 5.—*Data on 14 Patients Given USP Quinidine Sulfate**

Case	Age	Sex	Cause	Duration of Arrhythmia	Date of Conversion	Quinidine Level at Conversion (mcg per ml)	Quinidine Maintenance Levels (mcg per ml)	Drug and Dosage (mg)	NSR (Months)	Number of Conversion Attempts	Comments
1	53	M	ASHD, Emph., Thyrotoxic, AF	1 year	11/63		1.3; 2.4 3.3	QS 200 q8h	5	1	
2	51	F	RHD, MS, MR, AF	5 years	11/63		3.0; 3.4 1.0; 3.0 2.5; 3.3 1.4; 1.8 0.4	QS 200 q6h	12	1	
3	74	M	ASHD,MR, LVH, AS, AF	2 years	2/64	4.4		QS 200 q6h	1 wk.	1	Refibrillated 1 week. Femoral embolus 2 weeks.
4	84	F	ASHD, RHD, MS, MR, LVH	20 years	3/64	1.6		QS 200 q6h	1	1	Persistent nodal rhythm.
5	66	M	ASHD, MR, AF	2 years	1/64	6.2		QS 200 q6h			
6	75	M	ASHD, MR, AS, MI, LVH	3 years	1/64	7.0		QS 200 q6h			
							5.4; 6.8 6.3	QS 200 q6h	4	1	
							3.4; 4.8 5.4	QS 100 q6h			
7	50	M	HCVD, LVH, MI, AF	1 day	10/64	8.0		QS 400 q6h	5	1	
							1.2	QS 200 q6h			
8	57	F	RHD, LVH, MS, MR, AF	2 years	11/63		1.0; 2.4	QS 200 q8h	3	2	
9	73	F	Thyrotoxic ASHD, LVH, AS	2 years	2/64	2.2		QS 200 q6h	2		Refibrillated 4/64. Ventricular tachycardia with first shock.
10	79	M	ASHD, MR, LVH	6 months	11/63	1.2					
							1.8; 2.0 1.2; 1.8 2.0	QS 200 q6h	9	1	
11	78	M	ASHD, AF	16 years	4/64	5.4		QS 200 q6h			Refibrillated 5/64.
							2.2		1		
12	80	M	ASHD, MI, AF	2 years	4/64	1.6		QS 200 q6h	4		Intolerant. Died 8/64. QS discontinued 4/64.
13	57	F	RHD, MS, AI, LVH, AF	5 years	12/63	4.6		QS 200 q8h	2		Refibrillated 2/64.
14	44	M	RHD, MR, MS, LVH, Emph.	3 years	12/63	4.4		QS 200 q6h			
							8.5; 4.4 3.1; 3.0 3.4; 6.0		8	3	

*NSR is the period of follow-up with normal sinus rhythm. ASHD=arteriosclerotic heart disease; RHD=rheumatic heart disease; HCVD=hypertensive cardiovascular disease; Emph.=emphysema; MR=mitral regurgitation; MS=mitral stenosis; AS=aortic stenosis; AI=aortic insufficiency; MI=myocardial infarction; LVH=left ventricular hypertrophy; M=male; F=female.

taking USP quinidine sulfate and two were not receiving quinidine. Quinidex Extentabs® when given 300 mg every 12 hours appeared to be reliable and safe in maintaining adequate serum quinidine levels below toxicity. The ease of administration of a 12-hour schedule as opposed to a six-hour schedule with USP quinidine sulfate is a favorable consideration. In this study we made no attempt to either randomize or accurately compare the effectiveness of the two quinidine forms. As the study progressed the usefulness of the long-acting quinidine preparation became more apparent and it became our prophylactic agent of choice.

The problem of quinidine prophylaxis is only incompletely answered by this study. The maintenance of a normal sinus rhythm depends, among other things, on the competency of the sinus node. This study still leaves unanswered the question of which hearts will remain stabilized without quinidine prophylaxis. Of the 23 patients maintaining a normal sinus mechanism for three or more months, four without quinidine prophylaxis have maintained normal rhythms an additional nine to 15 months. One could then speculate that a good proportion of all patients (perhaps 15 per cent) might receive no additional benefit from quinidine prophylaxis following electrical conversion. Since in only one case in the present study was conversion attempted without quinidine, this might be worthy of a future investigation.

Quinidine has several pharmacologic effects. It inhibits the vagal influence on the sinus node, slows conduction through the myocardium and conducting tissues and decreases myocardial excitability. Because of these various effects on the heart, it would appear beneficial to maintain some permanent "safe" serum quinidine level following the conversion of arrhythmias. However, serious toxic reaction to quinidine is often demonstrated with serum quinidine concentrations greater than 6 mcg per ml.[9] In the present study 50 per cent of patients maintained a normal sinus mechanism for at least three months and 28 per cent for at least six months while receiving quinidine with serum levels less than 5 mcg per ml. It would, therefore, be reasonable to recommend serum quinidine levels of this magnitude for approximately six months after conversion, followed by a watchful waiting period without prophylaxis.

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